UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,658	06/23/2005	**Richard A Mathies**	UCALP031	5388

22434 7590 02/19/2008

BEYER WEAVER LLP
P.O. BOX 70250
OAKLAND, CA 94612-0250

EXAMINER	
KIM, YOUNG J	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
02/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,658	MATHIES ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-12 and 14-53* is/are pending in the application.

4a) Of the above claim(s) *27-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-12,14-26 and 37-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/5/07 & 12/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The present Office Action is responsive to the Amendment received on December 5, 2007.

Information Disclosure Statement

The IDS received on December 5, 2007 and December 26, 2007 are acknowledged.

Preliminary Remark

Claims 3, 4, and 13 are canceled.

Claims 27-36 remain withdrawn as being drawn to non-elected invention without traverse, as noted in the reply filed on May 18, 2007.

Claims 38-53 are new.

Claims 1, 5-12, 11-26, and 37-53 are under prosecution herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5-12, 14-26, and 37-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

Claims have been amended to recite the limitation, "one pneumatically actuated diaphragm pump."

While the specification appears to support for the limitation drawn to a pneumatically actuated valve, the specification does not appear to have any support for a pump that is pneumatically actuated.

Applicants are advised to either delete the new matters from the claims or specifically point out where in the specification such language is found.

Claim Rejections - 35 USC § 103

The rejection of claims 1-26, and 37 under 35 U.S.C. 103(a) as being unpatentable over Lagally et al. (Sensors and Actuators B, 2000, vol. 63, pages 138-146; IDS ref# C3[1]) in view of Waller et al. (Applied Environmental Microbiology, 2000, vol. 66, no. 9, pages 4115-4118), made in the Office Action mailed on July 2, 2007 is withdrawn in view of the Amendment received on December 5, 2007.

Specifically, none of the references disclose for at least one pneumatically actuated diaphragm pump which is integrated onto the microfluidic device.

Rejection, Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[1] In the IDS received on June 5, 2006.

Claims 1, 2, 5-12, 14-26, and 37-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (U.S. Patent No. 5,922,591, issued July 13, 1999) in view of Waller et al. (Applied Environmental Microbiology, 2000, vol. 66, no. 9, pages 4115-4118).

Anderson et al. disclose a target detection system, said system comprising:

a) a PCR chamber (column 2, lines 24-27; column 3, lines 33-37; column 9, lines 8-11);

b) a capillary electrophoresis (CE) mechanism (column 15, lines 33-38), and microchannels connecting various chambers (column 2, lines 35-40), wherein the fluid flow is controlled by pneumatically controlled valves (column 4, lines 55-56; column 29, lines 53-54).

With regard to claims 2 and 12, Anderson et al. disclose that their DNA analysis mechanism comprises PCR and CE (discussed above), wherein the artisans explicitly disclose that, "[m]icrocapillary array electrophoresis generally provides a rapid method for size based sequencing, PCR product analysis.." (column 15, lines 46-48).

With regard to claim 5 and 10, the chamber for PCR is disclosed as being used for amplification of DNA obtained from lysing the target of interest (column 6, lines 30-48).

With regard to claims 6 and 14, the capillary is etched microchannel (column 15, lines 63-67).

With regard to claims 7 and 15, the artisans also disclose the necessary step of desalting or purifying the extracted DNA (column 7, lines 17-36).

With regard to claims 23 and 24, the device chamber is formed on a glass layer (column 18, lines 60-63).

With regard to claim 25, the device disclosed by Anderson et al. comprises a plurality of channels (Figure 12C).

With regard to claims 26, 39, 43, 47, and 51, the pneumatic valves are controlled by vacuum (column 29, lines 54-57).

With regard to claims 38, 42, 46, and 50, the target is contemplated as being pathogens (column 6, line 33).

With regard to claims 41, 45, 49, and 53, the artisans employ their valves to direct the fluid directions (see Figure 12C, valves 1262, 1264, 1266, and 1268).

While Anderson et al. explicitly contemplate a microfluidic device which couples both PCR and CE analyses, the artisans are not explicit in stating that their device is adapted for conducting immunocapture (claims 1, 8, 9, 11, 16-22, 37, 40, 44, 48, and 52).

Waller et al. disclose a method of immunocapture PCR assay for the purpose of detecting a pathogenic species, *Campylobacter jejuni* from food samples (see Abstract).

Waller et al. explicitly disclose a step of binding *Campylobacter* in sample by adding polyclonal anti-*Campylobacter jejuni* IgG to the sample, followed by the purification of the antigen-antibody complex with anti-rabbit IgG-coated Dynabeads (page 4116, 1st column, 1st paragraph).

Waller et al. also disclose the step of lysing the captures cells, so as to remove the *C. jejuni* genomic DNA from the antigen-antibody complex, followed by the amplification of said genomic DNA in a PCR reaction (page 4116, 1st column, 2nd and 3rd paragraph).

Waller et al. evidences the well known practice of cleaning up and concentrating the isolated DNA prior to amplification procedure (page 4116, 1st column, 2nd column).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Anderson et al. with the teachings of Waller et al., thereby arriving at the invention as claimed for the following reasons.

Initially, the use of microfluidic device has been well-established in the art, the benefits of which would be certainly recognized by one of ordinary skill in the art, such as being able to conduct

series of biological reactions on a single device, resulting in efficiency, reduced chances of contamination, human errors, etc.

Additionally, the use of such microfluidic device for the purpose of detecting various target nucleic acids from a sample, be it for a certain medical condition (i.e., cancer) or for the presence of pathogens from samples, is also well known and recognized in the art of miniaturized biological device.

Whether one of ordinary skill in the art, at the time the invention was made would have been motivated to combine the teachings of Anderson et al. with the teachings of Waller et al. is the question in the present formulation of obviousness. It is respectfully submitted that one of ordinary skill in the art would have been certainly motivated to combine the teachings for the following reasons.

As previously stated, Anderson et al. disclose a microfluidic device, which is capable of amplifying and conducting electrophoresis of the amplified products

However, the amplification method employed by Lagally et al. is drawn to a PCR amplification, which has recognized deficiencies when it comes to the detection of pathogens, one of which is clearly and explicitly identified by Waller et al.:

> "Due to the prevalence of *Campylobacter* species in the food supply, routine and reliable monitoring for these pathogens is necessary in order to reduce their impact upon human health. Cultivation methods involving enrichment, isolation, and biochemical characterization require 4 to 5 days to comlete…Due to the perishable nature of many food items, a more rapid detection method is necessary to feasibly monitor the potential sources of theses pathogens. For this reason, we have developed an immunocapture PCR method for the detection of *Campylobacter* in foods." (page 4115, 1st column, bottom paragraph)

Hence, one of ordinary skill in the art would have had a clear motivation to fabricate a microfluidic device comprising an assay chamber(s) for conducting immunocapture of pathogens

from samples prior to the PCR and capillary electrophoretic analysis, thereby arriving at the invention as claimed.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at combining the immunocapture chamber coupled to PCR and CE mechanism, thereby arriving at the claimed device for the following reasons.

The art of microfluidic device has been well-established in the art, which enables an ordinarily skilled artisan to couple a plurality of biochemical reactions, including but not limited to sample purification, enrichment, lysis, amplification, hybridization, etc. (see Zanzucchi et al. patents for example[2]).

Hence, given the motivation provided for by Waller et al. which allows one of ordinary skill in the art to detect pathogens in a sample, wherein the artisans explicitly disclose the uses of antibody and bead assisted immunocapture of pathogens, followed by the lysis of the captured pathogens prior to amplification, one of ordinary skill in the art would have had a reasonable expectation of success at creating a chamber or chambers prior to the PCR-CE detection on the microfluidic device of Anderson et al.

Lastly, with regard to providing preconcentration and clean chambers in the device of Anderson et al., it would have been obvious in view of the fact that Waller et al. explicitly disclose the step of cleaning up and concentrating the DNA prior to its amplification. In addition, such practice would have been well within the purview of an ordinarily skilled artisan given the fact that PCR would have been more effective by removing the contaminating cell contents when lysing the pathogens in the sample.

---

[2] Zanzucchi et al. holds a plurality of patents which demonstrate feasibility of coupling a plurality of biochemical reactions in a microfluidic device, see for example, USPN 5,585,069 which was filed in November 1994.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 1-26 and 37 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-39 of copending Application No. 10/750,533 (herein, '533 application), made in the Office Action mailed on July 2, 2007 is maintained for the reasons already of record.

In addition, the newly submitted claims 38-53 are subject to the same provisional rejection as being necessitated by Amendment (by way of their addition).

Applicants state that the rejection will be addressed upon finding of otherwise allowable subject matter, in their response received on December 5, 2007.

As no claims are allowable and a terminal disclaimer had not been filed, the present rejection will be maintained for the reasons already of record.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the microfluidic device disclosed by '533 application also comprises sample delivery channels (bus) and chambers, for explicit, disclosed mechanism involving PCR and CE integrated thereto (see claim 34). While the claims of '533 application is silent with regard to the use of the device for the purpose of pathogen detection as well an immunocapture chamber, said modification is deemed obvious in view of the teachings of Waller et al. as discussed in the above rejection.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Applicant's arguments with respect to the previous rejections of record have been considered but are moot in view of the new ground(s) of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on

the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like

assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/
Primary Examiner, Art Unit 1637

/YJK/